1052-186 **Safety and Efficacy of Sirolimus-Eluting Stent (cypher) in Acute Myocardial Infarction: A substudy of the Rapamycin-Eluting Stent Evaluation at Rotterdam Cardiology Hospital (RESEARCH) Study**

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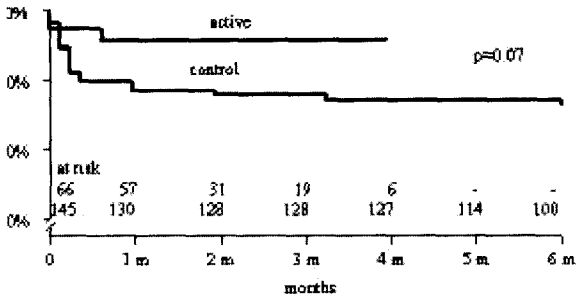
Background: Cypher stent reduces restenosis in stable pts with simple lesions. Our aim is to assess the safety and efficacy of cypher stent in AMI pts.
Methods: AMI pts admitted for PCI during the 6 mths period (16th Apr-15th Oct 02) were screened for eligibility for cypher stent. AMI pts who underwent PCI during the prior 6 mths (16th Oct 01-15th Apr 02) were recruited as historic control.
Results: Up to 27th Aug 02, totally 92 AMI pts (presented within 6 hrs) were screened and 66 (72%) were recruited (cypher gp). These 66 accounted for 17% of the 384 pts who were recruited in the RESEARCH study during the same period. Reasons for exclusion were stent diameter unavailable (n=17), length unavailable (n=1) or physician preference (n=8). Among pts (70% male) in the cypher gp, the average age was 66+/-14 yrs. Risk factors were smoking (24%), DM (7.6%), HT (52%), hypercholesterolemia (52%) and adverse family history (33%). Peak CK was 3367+/-2239 IU/L. Anterior MI accounted for 50% of infarction. Average 1.5 stents (1-5) were implanted per pt. Majority (80%) received 3-mm diameter stent. Post-procedural diameter stenosis by QCA changed from 80+/-20 to 11+/-5%. The procedural success rate was 92% with 8% failed to achieve TIMI 3 flow. Average follow-up period was 2.2 mths (2.0-4.5). There was no stent thrombosis. The cypher gp showed a positive trend towards reduction in repeat revascularization rate (figure).
Conclusion: Cypher stent is safe and effective in reducing the repeat revascularization rate in pts presented with AMI.



POSTER SESSION

1053 Percutaneous Intervention: Angiogenesis and Biologic Insights

Sunday, March 30, 2003, 3:00 p.m.-5:00 p.m.
McCormick Place, Hall A
Presentation Hour: 3:00 p.m.-4:00 p.m.

1053-173 **A Randomized Double Blind Placebo Controlled Multicenter Pilot Study of the Safety and Feasibility of Ad_{GV}VEGF121.10 via an Intramyocardial Injection Catheter in Patients With Advanced Coronary Artery Disease**

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Background: This phase 1, randomized, double blind, placebo controlled pilot study evaluated, for the first time, the safety and feasibility of percutaneous catheter-based delivery of an adenovector. Ad_{GV}VEGF121.10(AdVEGF), a replication-deficient adenovirus carrying the transgene encoding for VEGF121, was administered to patients with severly symptomatic coronary artery disease (CCS angina class III or IV) not amenable to conventional revascularization procedures.
Methods: Ten patients were randomized (2:1) to receive AdVEGF ($4X10^{10}$pu) or diluent (placebo), as fifteen 100μL endomyocardial injections, distributed evenly across the left ventricle using a non-flouroscopic, 3-dimensional mapping injection catheter system.
Results: Treatment was successfully administered in all cases. Median time of total catheterization procedure and from first to last injection was 2.5 hrs (range: 1.4 - 3.2 hrs) and 34 mins (range: 12 - 73 mins) respectively. One case of moderate vomiting and two cases of mildly elevated CPK (one AdVEGF and one placebo patient) were considered related to procedure. AdVEGF was well tolerated and only one treatment-related event, transient periprocedural fever, was observed. All adenoviral cultures (urine and throat swab) were negative, and no significant changes in plasma VEGF levels were noted. At up to 12 months follow-up, no cancers, proliferative retinal changes, or significant abnormalities in hepatic, renal or hematological indices were observed. At week 12, change from baseline in time to an additional 1mm ST depression on exercise ECG for AdVEGF group trended towards improvement, while the placebo group deteriorated slightly.
Conclusions: Catheter-based endomyocardial injection of AdVEGF is practical, feasible and safe, and is associated with no systemic viral distribution. A randomized, phase II 'proof-of-concept' study is warranted.

1053-174 **Effective Stent-Based Delivery of Tissue Inhibitor of Metalloproteinase 3 to Porcine Coronary Arteries Using a Novel Biosynthetic Stent Coating**

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Background: In-stent restenosis continues to pose a problem for the longterm success rate of percutaneous coronary intervention. We aimed to develop a suitable vehicle for the local delivery of a therapeutic adenovirus to coronary arteries, resulting in overexpression of Tissue Inhibitor of Metalloproteinase 3 (TIMP3). TIMP3 is known to induce apoptosis of vascular smooth muscle cells, thus reducing neointima formation.
Method: We used a Matrix HI phosphorylocholine coated (PC) stent (Biocompatibles, Farnham, U.K.), with enhanced cationic charge to increase viral transduction efficiency to porcine coronaries.
Preliminary studies to evaluate the coating & optimal viral dosing were performed with uncoated and PC-stainless steel coupons. Subsequently, stents pretreated with β-Galactosidase adenovirus, were implanted, invitro, in porcine coronary arteries & flushed with 1 of 5 solutions - no flush, 0.9% saline, contrast media, blood, or culture medium (n=5 for each group). The stented arteries were cultured for 48hours, fixed & stained with X-Gal to confirm viral transduction. Transduction was quantified 'en-face' using Image Pro. Invivo transduction was first assessed with β-Gal PC-stents in porcine coronaries & following this, TIMP3 stents were implanted for up to 7 days. Harvested tissues were analysed for presence of virus & gene product using PCR & immuno-histochemical methods.
Results: PC-stainless steel coupons showed superior β-Gal transduction rates compared to uncoated coupons. Invitro transduction rates were; No Flush 6.9+/-3.7%, 0.9% Saline 6.6+/-3.6, Culture Medium 7.2+/-2.5%, Contrast Medium 7.4+/-1.9%, & Blood 16.2+/-9.3%. Invivo, we demonstrated localized transduction of β-Gal, & more importantly, TIMP3 without systemic distribution of the virus, up to 7 days after implantation.
Conclusion: Our results demonstrate effective, in-vitro & in-vivo, transduction of adenovirus from a stent using a novel biosynthetic coating, already licensed in humans. Additionally, we demonstrated effective & localised production of TIMP3 in stented coronaries. The combination of TIMP3 & a PC stent is a potentially attractive candidate for the prevention of in-stent restenosis.

1053-176 **Endovascular Cryotherapy Increases Luminal Area in the Focally Atherosclerotic Hypercholesterolemic Rabbit**

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Background: There is recent interest in the use of cryotherapy to treat atherosclerotic lesions. The objective of this study was to characterize the effects of endovascular cryotherapy on vessel wall components in the hypercholesterolemic, focally atherosclerotic rabbit.
Methods: Bilateral focal femoral atherosclerosis was induced by air desiccation in twenty New Zealand White rabbits. Animals were then placed on a 0.5% cholesterol diet for 28 days. Utilizing a cryo-balloon system, vessels underwent a sham procedure (n=10) or cryotherapy at 4 temperatures: -20°C(n= 4), -10°C(n=8), 0°C(n=8), and +10°C(n=10). Animals were placed on a chow diet for 28 days post cryotherapy at which time animals were euthanized and arteries harvested for analysis.
Results: Vessels treated at +10°C had significantly larger external elastic lamina (EEL) and luminal area (2.13±0.12 mm^2 vs. 1.23±0.16 mm^2, p=.0004; 0.85±0.10 mm^2 vs. 0.51±0.12 mm^2, p=.04) together with a higher macrophage content and lower total vessel collagen content compared with sham controls (50.4±4.9 % vs. 26.75±6.9 %, p=.01; 52.3±3.3 % vs. 64.0±3.2 %). Vessels in the other groups were not different from sham controls although a trend for larger EEL area (1.78±0.25 vs. 1.23±0.16 mm^2, p=.07) and a trend for increased neointimal/medial collagen content (44.7±6.8% vs. 32.6±4.9%, p=.15) were seen at −10°C. The cross sectional area of narrowing by plaque (CSAN-P) and smooth muscle cell content were similar among groups.
Conclusions: Endovascular cryotherapy at +10°C significantly increases luminal and EEL area of focally atherosclerotic arteries without a change in CSAN-P, consistent with a positive remodeling effect. Furthermore, there were more macrophages and less collagen deposition in these vessels, which may have facilitated positive remodeling. A trend for increased EEL area was also seen at −10°C as well as increased collagen content in the neointima and media, which may enhance plaque stability. Further studies of this novel technique utilizing various treatment temperatures and regimens are currently in progress.